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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/808,827	02/28/1997	WALTER HENRY GUNZBURG	GSF97-01A	6837

21005 7590 06/17/2003

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EXAMINER
BRUSCA, JOHN S

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	08/808,827	SALLER ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communicati n appears on the cover sheet with the c rresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1,5,7,9-26,28,29 and 31-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7,9-26,28,29 and 31-101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 1997* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. It is brought to the applicant's attention that throughout the arguments filed 16 May 2003 the applicants refer to instant claim limitations "said promoter regulating , after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences" which is not present in the instant claims due to the amendment filed 16 May 2003. The claims as amended have been examined.

Drawings

2. New corrected drawings are required in this application because of the deficiencies noted in the draftspersons patent drawing review attached to the Office action mailed 18 April 2000. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 16 May 2003 has been entered.

Claim Rejections - 35 USC 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

> pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 5, 7, 9-26, 28, 29, 31, 32, and 56-78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite the phrase "a heterologous promoter other than a promoter from a retrovirus upon which the retroviral vector is based or a promoter from a subtype of the retrovirus upon which the retroviral vector is based." The applicants have failed to note support for the amendment as required in MPEP 714.02 and 2163.06. A review of the specification does not reveal subject matter that supports the amendment recited above. While the specification provides an example of insertion of a promoters from a cellular gene, it does not provide support for the claimed genus of retroviral promoters.

Applicant's arguments filed 16 May 2003 have been fully considered but they are not persuasive. The applicants point to description of one promoter, MMTV, which they assert is a member of the claimed genus. For the reasons discussed below the metes and bounds of the limitation are indefinite and it is not clear whether MMTV promoters are members of the claimed genus. The Applicants have failed to a description of the claimed genus of promoters in the instant specification at the time of filing. As such the rejection is maintained.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 5, 7, 9-26, 28, 29, and 31-101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 5, 7, 9-26, 28, 29, 31, 32, and 56-78 are indefinite for recitation of the phrase "a heterologous promoter other than a promoter from a retrovirus upon which the retroviral vector is based or a promoter from a subtype of the retrovirus upon which the retroviral vector is based" because the metes and bounds of the claimed promoter are unclear.

Applicant's arguments filed 16 May 2003 have been fully considered but they are not persuasive. The applicants have failed to define the metes and bounds of the claimed genus of promoters.

Claims 1, 5, 7, 9-26, 28, 29, and 31-101 recite the limitation "said one or more sequences selected from coding sequences." There is insufficient literal antecedent basis for this limitation in the claim. The rejection would be overcome by amending the independent claims to be drawn to only coding sequences throughout each independent claim.

Claims 1, 5, 7, 9-26, 28, 29, and 31-101 are indefinite because they read on vectors that comprise only non coding sequences that further comprise promoters that regulate only coding sequences. The rejection would be overcome by amending the independent claims to be drawn to only coding sequences throughout each independent claim.

Claims 1, 5, 7, 9-26, 28, 29, 31, 32, and 56-78 are indefinite for recitation of the phrase "reduced chance of recombination" because the metes and bounds of the limitation are not clear. It is not known what the claimed level of recombination is or what the reduced chance is relative to.

Claim Rejections - 35 USC 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Couture et al. in view of Faustinella et al.

Couture et al. (Reference AS in the Form PTO-1449 filed 9/23/97) shows retroviral vectors comprising a substitution of a portion of the 3' U3 region with the corresponding region of 5 different murine retroviruses, including leukemia and sarcoma retroviruses. Couture et al. shows on page 669 column 2 that the first 40 nucleotides of the original vector are retained in the substitution of the U3 region. The vector of Couture comprises a chloramphenicol acetyl

transferase marker gene and a neomycin resistance gene. Couture et al. shows in the abstract that after packaging, the substituted U3 region appears at the 5 LTR and serves as a promoter for all genes in the body of the vector, and that different LTR constructs were preferentially expressed in specific cell types. Couture et al. states in the second paragraph of the Results section on page 669 that U3 regions are bound by cellular factors. Couture et al. shows in Table 3 that their chimeric LTR promoters are active in a cell type specific manner. Couture et al. state on page 670 that promoter suppression or interference may occur within retroviral vectors containing internal promoter elements. Couture et al. states on page 667 that retroviral vectors with target cell specificity have utility in gene therapy protocols. Couture et al. shows the use of packaging cell lines PA317 and GP&E86 on page 669 to package their retroviral vectors. Couture et al. does not show a vector comprising a multiple cloning site in the U3 region.

Faustinella et al. shows in figure 1 Moloney murine leukemia retroviral vector pS3. pS3 comprises a partial deletion of the 3 U3 region, into which has been inserted a polylinker with unique cloning sites, for example the Bsa AI site and the Nae I site used to construct the vectors of figure 2.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the vectors of Couture et al. by adding the multiple cloning site of Faustinella et al. because Faustinella et al. shows that multiple cloning sites may be used to insert sequences of choice in a U3 region of a retroviral vector.

10. Claims 1, 5, 7, 9, 11, 12, 16-25, 28, 29, 31, 32, 56-59, 61, 62, 65-72, and 74-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Couture et al. in view of Faustinella

et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above, and further in view of Mee et al.

Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above does not show mouse mammary tumor virus (MMTV) promoters or regulatory elements.

Mee et al. shows a retroviral vector comprising a mouse mammary tumor virus LTR, and that the LTR expressed a gene after induction with dexamethasone. Mee et al. state on page 292 that their vector is a potentially powerful tool for the manipulation of gene expression in a variety of cell types.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the vector of Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above by insertion of an MMTV promoter region in a deleted 3' U3 region of a retroviral vector because Mee et al. show that their LTR promoter may be used to manipulate gene expression in a variety of cell types.

11. Claims 1, 5, 7, 9, 11, 12, 15-25, 28, 29, 31-35, 38, 39, 42-49, 51-55, 79-82, 84, 85, 88-95, and 97-101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above, and further in view of Mehigh et al.

Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above does not show cellular promoters or regulatory elements.

Mehigh et al. shows a retroviral vector comprising a whey acidic acid protein (WAP) promoter. Mee et al. states in the abstract that their vector allows for inducible expression from the WAP promoter of an operably linked gene in MBDK cells and may prove useful as a delivery system for peptides in cattle to increase milk production.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the vector of Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above by insertion of a WAP promoter region in a deleted 3' U3 region of a retroviral vector because Mehigh et al. shows that such vectors are inducibly expressed and may allow for increased milk production in cattle.

12. Claims 1, 13, 14, 33, 40, 41, 56, 63, 64, 79, 86, and 87 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of:

1)Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above,

2)Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above, and further in view of Mee et al. as applied to claims 1, 5, 7, 9, 11, 12, 16-25, 28, 29, 31, 32, 56-59, 61, 62, 65-72, and 74-78,

3) Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above, and further in view of Mehigh et al. as applied to claims 1, 5, 7, 9, 11, 12, 15-25, 28, 29, 31-35, 38, 39, 42-49, 51-55, 79-82, 84, 85, 88-95, and 97-101,

and further as evidenced by Miller et al. and Panganiban et al.

The three combinations of references cited above do not explicitly show an altered retroviral gene or a partially deleted sequence involved in integration of retroviruses.

Couture et al. shows in figure 1 a retroviral vector LCSN and a derivative of LCSN. Couture et al. shows in the Methods section on page 668 that their vectors are derivatives of the vectors of Miller et al.

Miller et al. shows in figure 2 that their vectors retain the phi+ packaging sequence, but lack the gag, pol, and env genes of a replication-competent retrovirus.

Panganiban '84 shows that the 3' end of the pol gene encodes the int locus that is required for integration of the reverse transcribed retroviral genome to form a provirus.

Therefore the vectors of claims 13 and 14 are taught by the above cited combinations of references as evidenced by Miller et al. and Panganiban et al.

13. Claims 1, 10, 33, 37, 56, 60, 79, 83, 89, and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of:

1)Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above,

2)Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above, and further in view of Mee et al. as applied to claims 1, 5, 7, 9, 11, 12, 16-25, 28, 29, 31, 32, 56-59, 61, 62, 65-72, and 74-78,

3) Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above, and further in view of Mehigh et al. as applied to claims 1, 5, 7, 9, 11, 12, 15-25, 28, 29, 31-35, 38, 39, 42-49, 51-55, 79-82, 84, 85, 88-95, and 97-101,

and further in view of Price et al.

The three combinations of references cited above do not explicitly show retroviral vectors derived from BAG vectors.

Price et al. shows a BAG retroviral vector comprising a beta galactosidase reporter gene, and that the vector can be used to identify cells and progeny of cells infected with the vector.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the vector of the above cited combinations of references by basing the construction on a BAG vector of Price et al. because Price et al shows that a vector with a beta-galactosidase reporter gene may be used to identify cells and progeny of cells infected with the vector.

14. Claims 17, 20, 21, 26, 28, 43, 50, 51, 52, 53, 66, 73, 74, 75, 76, 89, 96, 97, 98, and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of:

1)Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above,

2)Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above, and further in view of Mee et al. as applied to claims 1, 5, 7, 9, 11, 12, 16-25, 28, 29, 31, 32, 56-59, 61, 62, 65-72, and 74-78,

3) Couture et al. in view of Faustinella et al. as applied to claims 1, 5, 9, 11, 1216-25, 28, 29, 31, 32, 56, 57, 59, 61, 62, 65-72, and 74-78 above, and further in view of Mehigh et al. as applied to claims 1, 5, 7, 9, 11, 12, 15-25, 28, 29, 31-35, 38, 39, 42-49, 51-55, 79-82, 84, 85, 88-95, and 97-101,

and further in view of Longmore et al. and Kay et al.

The three combinations of references cited above do not show use of retroviruses in animals.

Longmore et al show in the abstract that mice infected with a retroviral vector expressing the erythropoietin receptor had increased platelet counts and splenic megakaryocytes.

Kay et al. shows in the abstract and throughout that hemophiliac dogs infected with a retroviral vector expressing factor IX shows improved levels of clotting and thromboplastin times for greater than 5 months after treatment.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the teachings of the combinations of references cited above to express a therapeutic protein because both Kay et al. and Longmore et al. show that retroviral vectors may be used to express therapeutically effective levels of a recombinant protein in an animal.

15. Applicant's arguments filed 16 May 2003 have been fully considered but they are not persuasive.

The applicants state that Couture et al. teaches away from the use of heterologous promoters, however Couture et al. shows that a variety of heterologous promoters have activity in the exemplified vectors (see tables 1-3).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 703 308-4231. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703 308-4025. The fax phone numbers for the organization where this application or proceeding is assigned are 703 746-5137 for regular communications and 703 746-5137 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

John S. Brusca
Primary Examiner
Art Unit 1631

jsb
June 14, 2003